

REMARKS

Upon entry of the above amendment, the claims will be 42, 44 to 51, 54 to 59 and 61.

Undersigned acknowledges with appreciation the indication that claims 44 to 48 are allowable, and that claims 55, 56 and 58 would be allowable if rewritten in independent form. However, for reasons set forth below, it is considered that all of the claims in this application are now in condition for allowance.

With regard to the rejection of claims 41, 43, 52, 60 and 62, such rejection is rendered moot by the cancellation of these claims.

Claims 42 and 61, and also claims 49, 50, 51, 54 and 57 dependent thereon, have been rejected as unpatentable over Dattagupta in view of Gingeras.

This rejection is respectfully traversed.

Dattagupta teaches the concept of a reverse dot-blot assay for the detection of a nucleic acid, by immobilizing one or more oligonucleotides and applying thereto a labelled polynucleotide target. Immobilization of oligonucleotide probes by covalent links is envisaged (page 9, lines 25 to 33), but there is no detailed chemistry.

Gingeras describes a sandwich assay involving the use of two oligonucleotide probes, of which one is immobilized on a support. Techniques for immobilizing pre-synthesized oligonucleotides on supports by means of covalent links through

terminal nucleotide residues are described. However, each oligonucleotide probe is pre-synthesized and provided in solution from which it is immobilized on a support. There is no teaching or suggestion to synthesize the oligonucleotide *in situ* on the surface of a support.

Applicant's claims 42 and 61 recite an array of oligonucleotides, each one of which has been pre-synthesized on the surface of the support, and are unobviously distinguished by virtue of this feature over Gingeras.

It may also be noted that the supports used by Gingeras are all particulate. Gingeras contains no teaching or suggestion to use a flat surface as a support, nor to form an array of oligonucleotides on a single surface.

Thus, as a reference against applicant's claims 42 and 61, Dattagupta is deficient in not teaching an array in which the oligonucleotides of each cell have been synthesized *in situ* and are attached to a surface of a support through a covalent linkage. And Gingeras by no means makes good that deficiency. Claims 41 and 62 are thus clearly unobvious over the cited prior art. Claims 49, 50, 51, 54 and 57 are dependent upon these two claims and should be allowed with them.

The *in situ* synthesis feature has real significance. It is important for practical operation of applicant's invention that a single mismatch (between an immobilized oligonucleotide of an array and a polynucleotide target) have a substantial destabilizing effect on the duplex. The extent of this

destabilizing effect depends on various factors, including the lengths of the oligonucleotide probes and the position of the mismatch in them.

Applicant's technique of synthesizing oligonucleotide probes *in situ* on a surface in the form of an array ready for use also has very significant advantages: the length of each oligonucleotide can be precisely controlled and varied; the position of a prospective mismatch can be controlled; these variables can readily be adjusted to determine the optimum conditions for efficient operation. All of these concepts are completely absent from the Dattagupta and Gingeras references, alone or combined.

For the above reasons, the rejections on prior art are clearly untenable.

No further issues remaining, allowance of this application is respectfully requested.

If the Examiner has any comments or proposals for expediting prosecution, he is invited to contact the undersigned at the telephone or facsimile number below.

Respectfully submitted,

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